TRANSMITTAL OF APPEAL BRIEF

Docket No.
LOREAL 3.0-039

In re Application of: Hani Fares, Marc Cornell, Sidney Peter Foltis, and Isabelle Hansenne

Application No.	Filing Date	Examiner	Group Art Unit
10/646,300	August 22, 2003	L. M. Williams	1617

Invention: COMPOSITIONS CONTAINING TOPICAL ACTIVE AGENTS AND PENTYLENE GLYCOL

TO THE COMMISSIONER FOR PATENTS:

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Dated: November 18, 2008

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Dated: November 18, 2008 Signature: _____ (Stephen J. Brown)

Docket No.: LOREAL 3.0-039

(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Fares *et al.*

Application No.: 10/646,300 Group Art Unit: 1617

Filed: August 22, 2003 Examiner: L. M. Williams

For: COMPOSITIONS CONTAINING TOPICAL ACTIVE AGENTS AND PENTYLENE GLYCOL

APPEAL BRIEF

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Appellants hereby file this brief to appeal from the final rejection of claims 16-38 mailed April 16, 2008. The Commissioner is hereby authorized to charge the fee required by 37 C.F.R. § 41.20(b)(2) for the filing of the brief. The Commissioner is also hereby authorized to charge any other fees that may be due and owing in connection with this appeal to Deposit Account No. 12-1095.

I. REAL PARTY IN INTEREST

The real party in interest is L'Oréal S.A., a corporation of France, having a place of business at 14 Rue Royale, 75008, Paris, France.

II. RELATED APPEALS AND INTERFERENCES

None. Appellants and their legal representatives and assignee are not aware of any other appeals, interferences, or judicial proceedings that may be related to, directly affect, or

be directly affected by or have a bearing on the Board's decision in the present appeal.

III. STATUS OF CLAIMS

Claims 1-15 have been canceled, claims 16-40 are pending in this application, and claims 39-40 have been withdrawn from consideration. Claims 16-38 have been finally rejected and are the subject of the present appeal.

IV. STATUS OF AMENDMENTS

None. No amendment was filed subsequent to the final rejection of the claims.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The claimed subject matter of the present application relates generally to the topical application of the steroidal hormone or anti-inflammatory agent hydrocortisone, and in particular in cosmetic or dermatological compositions which are superior to those previously used in view of the inclusion of pentylene glycol therein.

With respect to the claims on appeal (*i.e.*, claims 16-38), claims 16 and 35-38 are independent. A concise explanation of each of these independent claims involved in the appeal is provided below (37 C.F.R. § 41.37(c)(v)).

Claim 16 is directed to a cosmetic or dermatological composition comprising: hydrocortisone, or a derivative thereof (¶ [0007] ll.1-3), and a solvent for said hydrocortisone comprising pentylene glycol (¶ [0004] ll.4-5), wherein said hydrocortisone is present in an amount of about 0.01% to about 5% by weight of said composition (¶ [0012] ll.9-12).

Claim 35 is directed to a method of formulating hydrocortisone or a derivative thereof for use in a cosmetic or dermatological composition (¶ [0007] ll.1-3), comprising: mixing (¶ [0005] ll.1-5) said hydrocortisone in an amount of about 0.01% to about 5% by weight of the composition

(¶ [0012] ll.9-12), and a solvent for said hydrocortisone comprising pentylene glycol (¶ [0004] ll.4-5).

Claim 36 is directed to a method of formulating a hydrocortisone or derivative thereof for use in a cosmetic or dermatological composition (¶ [0007] ll.1-3), comprising: mixing (¶ [0005] ll.1-5) said hydrocortisone or a derivative thereof in an amount of about 0.01% to about 5% by weight of the composition (¶ [0012] ll.9-12), and a solvent for said hydrocortisone comprising pentylene glycol (¶ [0004] ll.4-5).

Claim 37 is directed to a method of treating skin or scalp, comprising: applying to skin or scalp (¶ [0006] ll.1-4) a composition comprising hydrocortisone or a derivative thereof (¶ [0007] ll.1-3), and a solvent comprising pentylene glycol (¶ [0004] ll.4-5), wherein said hydrocortisone is present in an amount of about 0.01% to about 5% by weight of said composition. (¶ [0012] ll.9-12).

Claim 38 is directed to a method of treating skin or scalp, comprising: applying to skin or scalp (¶ [0006] ll.1-4) a composition comprising hydrocortisone or a derivative thereof (¶ [0007] ll.1-3), and a solvent for said hydrocortisone comprising pentylene glycol (¶ [0004] ll.4-5), wherein said hydrocortisone is present in an amount of about 0.01% to about 5% by weight of said composition (¶ [0012] ll.9-12).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether claims 16-38 are obvious over Castro *et al.*, U.S. Patent 6,113,888 ("*Castro*"), in view of Cooper *et al.*, U.S. Patent 4,552,872 ("*Cooper*"), in view of Quigley *et al.*, U.S. Patent 6,075,056 ("*Quigley*"), in further view of Vollhardt, U.S. Patent 6,274,124 ("*Vollhardt*").

VII. ARGUMENT

A. Synopsis of Argument

Appellants respectfully submit that the Examiner has repeatedly refused to even consider the clear evidence of unexpected results contained in the Specification and the Fares Declaration.[1] Indeed, the Examiner appears to believe that evidence of unexpected results, if set forth in the specification itself, is of little or no value. Having ignored this evidence, the Examiner then fails to offer any facts or reasoning as to why this evidence is insufficient to overcome a *prima facie* case for obviousness. Accordingly, the evidence of unexpected results stands completely unrebutted, and Appellants respectfully submit that they have demonstrated that the claimed invention is not obvious and is a patentable contribution over the prior art.

Irrespective of the above, however, and even if one ignores this evidence of unexpected results, the Examiner's alleged *prima facie* case is insufficient on its face. This rejection is thus based on a primary reference ("*Castro*") which literally discloses thousands of possible combinations and sub-combinations of optional ingredients, and requires the random selection of certain of these ingredients, for no apparent reason apart from knowledge of Appellants' invention. Since there is no logical reason to do so — indeed, there are reasons within this reference itself for not doing so — the lynchpin of the Examiner's entire case is faulty.

Moreover, the cited combination of references disclose widely disparate compositions and methods, which are directed to purposes that are completely incompatible with one another. The Examiner suggests combining these references. Combining these

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[1] Declaration under 37 C.F.R. § 1.132 of Hani Fares, Ph.D. submitted to the Office on March 29, 2005 ("the Fares Declaration"). A copy has been provided in the Evidence Appendix.

references, however, would render one or more of them unsatisfactory for their intended purposes. Such a combination cannot meet the Examiner's burden to establish a *prima facie* case for obviousness.

In making the rejection, the Examiner has thus relied on only those portions of the cited references which support his position, and apparently ignored the remainder of these disclosures. When the disclosures of the cited references are read in their entireties, however, there is nothing that would motivate one of skill in the art to combine these references in the manner suggested by the Examiner. For this additional reason, Appellants respectfully submit that the rejection fails to present a *prima facie* case for obviousness.

B. The Cited References

Castro is primarily directed to "a composition comprising a self-tanning agent, a nitrogen-free polymer, and a nitrogen-free surfactant" (col.1 ll.40-42), none of which constitute the required elements of the present invention. *Castro* discloses that the "polymer and surfactant . . . help stabilize the active self-tanning agent . . . ." (col.3 ll.11-12), and defines a "self-tanning agent" as "a chemical agent capable of producing or inducing the artificial tanning process of the skin by forming brown pigments in the skin, *e.g.*, through the Maillard reaction . . . ." (col.3 ll.15-19). Without going into detail, topical self-tanning agents, such as those preferred by *Castro* (*i.e.*, 1,3-dihydroxyacetone and 1,3,4-trihydroxy-2-butane), react with the amino acid groups of the proteins in the dead skin surface layer (stratum corneum) to form pigments called melanoidins, which mimic a tan. These topical self-tanning agents do not penetrate beyond the surface layer of the skin.

Castro also discloses that its composition may be in a cosmetic product including a cosmetically acceptable carrier, "the individual components of [which] are numerous and varied," and are thus optional ingredients in the context of this reference. These include over 20 separate classes of such components (col.3 ll.39-51), followed by pages of specific examples of each such class of these optional ingredients. Two of these disclosed classes are dermatologically active agents and humectants. Over 60 dermatologically active agents are specifically disclosed, including hydrocortisone. (Col.4 l.64 to col.5 l.16.) Fourteen specific humectants are disclosed, including 1,2-pentanediol. (Col.5 ll.49-54.) *Castro*, however, does not disclose any composition containing 1,2-pentanediol and hydrocortisone, and even the Examiner must admit that it would be serendipitous for one to somehow even select these two classes of components, much less the specific ingredients constituting the presently claimed invention.

Turning to the secondary references, *Cooper* is directed to "improved compositions and methods for the percutaneous delivery of corticosteroids . . . . The compositions of this invention comprise a safe and effective amount of a corticosteroid, together with a penetration-enhancing vehicle containing a C_3-C_4 diol, such as propylene glycol, and a cell-envelope disordering compound, such as oleic acid . . . ." (Col.5 ll.6-21.) *Cooper* discloses that "[t]he vehicles of the present invention . . . comprise, at a minimum, a diol and a cell-envelope disordering compound." (Col.8 ll.52-55.)

Cooper then discloses that the "diol compounds useful in the compositions and methods of the instant invention include 1,2-propanediol, 1,3-propanediol, 1,2-butanediol, 1,3-butanediol, 1,4-butanediol, or mixtures of these diol compounds." (Col.8 ll.56-60.) *Cooper* discloses "Penetration Studies demonstrat[ing] . . . the ability of the compositions of

the present invention to enhance penetration of triamcinolone or hydrocortisone when compared to a propylene glycol or a propylene glycol-containing vehicle formulated without the presence of the critical cell-envelope disordering compound." (Col.15 ll.23-31.) Cooper utterly fails to disclose pentylene glycol.

Quigley discloses a "stable topical formulations comprising an antifungal agent and an antiinflammatory steroid." (Col.1 ll.6-7.) Among the antiinflammatory steroids disclosed is hydrocortisone. (*See* col.4 l.53 to col.5 l.62.) *Cooper* discloses that its topical formulations may include pharmaceutically acceptable excipients, including solvents. (Col.2 ll.53-55.) Among the disclosed solvents are glycols: "propylene glycol, butylene glycol, hexylene glycol, polyethylene glycols, [and] polypropylene glycols." (Col.2 ll.55-57.) Again, pentylene glycol is not even referred to therein.

Quigley discloses that a disadvantage of previous topical antifungal combinations "is that it is undesirable to use steroids for topical treatment for extended periods of time. Steroids can penetrate the skin and cause undesirable side effects, including skin atrophy, suppression of the hypothalamic-pituitary-adrenal axis, Cushing's syndrome, glucosuria, hyperglycemia, etc." (Col.1 ll.27-32.) *Quigley* discloses that the advantages of its formulation include that: 1) "the combination of the antifungal agent and the steroid demonstrates a synergistic effect, . . . [and therefore] the time is greatly reduced for alleviation of the symptoms and for complete eradication of the disease . . .," and 2) "it delivers the antifungal agent and the steroid to the skin, but minimizes the penetration of the skin with respect to the steroid, thus avoiding the potential side effects attendant upon prolonged steroid use." (Col.2 ll.16-27.)

Finally, *Vollhardt* discloses a "method for imparting water resistance to or improving water resistance of a cosmetic or dermatological formulation, comprising adding an water resistance enhancing effective amount of 1,2-pentanediol . . . ." (Abstract.) *Vollhardt* is primarily directed to sunscreen compositions, but also discloses other cosmetic and/or dermatological active agents, including "steroidal anti-inflammatory agents such as hydrocortisone . . . ." (Col.4 ll.53-67.) *Vollhardt*, however, does not disclose any composition containing 1,2-pentanediol and hydrocortisone.

Vollhardt discloses that "1,2-pentanediol is characterized by a virtually unlimited miscibility with water. Thus, it was absolutely unexpected that 1,2-pentanediol can improve the water resistance of a cosmetic or dermatological formulation." (Col.3 ll.40-43.) *Vollhardt* also discloses that other glycols, such as, "1,2-propanediol and 1,2-hexanediole do not show a water resistance enhancing effect [and] . . . hexandiole rather decreases the water resistance of a cosmetic formulation." (Col.3 ll.46-50.)

C. The Examiner's Position

The Examiner has taken the position that:

> [*Castro*] discloses topical compositions comprising 1,2-pentanediol, an additional glycol (2-methyl-1,3-propanediol), and a dermatologically active agent (which could be hydrocortisone or triamcinolone). [*Cooper*] discloses topical pharmaceutical corticosteroid compositions including 1,2-propanediol, 1,3-propanediol, 1,2-butanediol, 1,3-butanediol, 1,4-butanediol or mixtures of these diols . . . [and] that the topical pharmaceutical corticosteroids used in the compositions include hydrocortisone, hydrocortisone butyrate, hydrocortisone acetate, triamcinolone, and triamcinolone acetonide. [*Quigley*] teach topical formulations of triamcinolone acetate and propylene glycol. [*Vollhardt*] teaches cosmetic and/or dermatological formulations comprising 1,2-pentanediol and at least one cosmetic or

> dermatological active agent in a cosmetically and/or pharmaceutically acceptable carrier for topical application to the skin[,] . . .that the cosmetic or dermatologically active agent can be a steroidal anti-inflammatory such as hydrocortisone . . . [and] that 1,2-pentanediol confers greater water resistance to compositions.

(Paper No. 20080325, at 7-8.)

The Examiner concludes that:

> [i]t would have been obvious . . . that 1,2-pentanediol could be used in the topical pharmaceutical corticosteroid compositions of Cooper *et al.*, in view of Vollhardt, as Castro *et al.* demonstrated that 1,2-pentanediol could be combined with another diol (propylene glycol or butylenes glycol or both) and that Castro *et al.*, Cooper *et al.* and Vollhardt's compositions all contain the same dermatologically active agents (steroidal anti-inflammatories) [and] Quigley *et al.* demonstrate that triamcinolone acetate is an acceptable steroidal anti-inflammatory for glycol formulations. The increased water resistance properties of 1,2-pentanediol containing compositions would motivate one of ordinary skill in the art to combine the compositions. A reasonable chance of success would be expected as the compositions demonstrate that 1,2-pentanediol can be combined with additional diols and all the compositions detailed include steroidal anti-inflammatory agents exemplified by hydrocortisone.

(*Id.* at 8-9.)

D. Both The Specification And The Fare's Declaration Present Unexpected Results Which Stand Unrebutted by the Examiner

Even assuming, *arguendo*, that a *prima facie* case of obviousness has been established, the Appellants have presented evidence of unexpected results both in the Specification and in the Fares Declaration. In particular, it has been demonstrated that the claimed compositions exhibit unexpectedly better aesthetic appeal, less tackiness, and greater bioavailability of the steroid. The Examiner has repeatedly failed to offer any explanation as to why this evidence is not sufficient to

overcome a *prima facie* case for obviousness. Indeed, the Examiner has not even referred to this data, as though its being in the specification somehow renders it of no moment. Having demonstrated, however, that unexpected results (which stand completely unrebutted), exist here, Appellants respectfully submit that they have more than demonstrated that the claimed invention is not obvious and constitutes a patentable contribution over the prior art.

Objective evidence of secondary considerations, *e.g.*, unexpected results, is relevant to the issue of obviousness, and such evidence must be considered in every case in which it is submitted, regardless of whether it is presented in the specification, by counsel or via affidavit or declaration. *See* M.P.E.P. § 2145, at 2100-162 (*citing In re Soni*, 34 U.S.P.Q.2d 1684, 1687 (Fed. Cir. 1996) (error not to consider evidence presented in the specification)). Moreover, if the Examiner finds the evidence insufficient to rebut the *prima facie* case of obviousness, it is his obligation to explain this determination. *See* M.P.E.P. § 2145, at 2100-164 ("Office personnel should not . . . summarily dismiss [rebuttal evidence] as not compelling or insufficient. If the evidence is deemed insufficient to rebut the *prima facie* case of obviousness, Office personnel should specifically set forth the facts and reasoning that justify this conclusion.").

In four different amendments, the Appellants have pointed to the evidence of unexpected results presented in the Specification. Moreover, in a declaration submitted on March 29, 2003, Dr. Hani Fares, a co-inventor of the present invention, has explained why he believes these results would not have been expected based on the collective teachings of the cited prior art. As described in the Specification, the claimed invention achieves several unexpected results. These results flow from Appellants' unexpected discovery that hydrocortisone

and its derivatives are more soluble in pentylene glycol than other polyols such as glycerol, propylene glycol, butylene glycol, and hexylene glycol, as disclosed in *Quigley* and *Cooper*.

More specifically, as shown in Example 1 on page 11, Appellants have discovered that hydrocortisone is about two times more soluble in pentylene glycol than in hexylene glycol, about 1.5 times more soluble in pentylene glycol than in propylene glycol, and about 1.25 times more soluble in pentylene glycol than in butylene glycol. There are no teachings or suggestions in any of the cited references to these effects. As taught in the present specification, there are at least three unexpected benefits that flow from the combination of pentylene glycol and hydrocortisone and its derivatives, namely aesthetic appeal, less tackiness, and greater bioavailability. The first two advantages are described on pages 5-6 of the specification as follows:

> Due to the greater solubility of the active agents in pentylene glycol, the amounts of the other solvents are significantly lower, *e.g.*, about 20 to 95 percent less than if pentylene glycol were not present. Relatively high amounts of glycols are undesirable from several standpoints, especially in terms of aesthetic appeal and tackiness. In contrast, compositions of the present invention are more aesthetically acceptable and have less tackiness.

In Example 7 on pages 16-18 of the specification, Appellants compared the rate of release of hydrocortisone from various commercially available one percent hydrocortisone anti-itch creams and ointments. The results clearly demonstrate that the release rate of hydrocortisone from a gel of the present invention was about 100 times greater than the various commercial products tested, none of which contains pentylene glycol. As described in paragraph 34 on page 18, and illustrated in Fig. 1, the results also show that the compositions of the present invention provide greater

availability of the active agent to penetrate the affected area on the skin or scalp, and thus provide greater bioavailability of the active agent.

As attested to by Dr. Fares, the results would not have been expected based on the collective teachings of the prior art. By specifically limiting the diols to C_3, C_4 and/or C_6 diols, *Cooper* and *Quigley* are believed to teach away from the claimed invention. *Vollhardt*'s primary objective was to increase water resistance or in other words, the amount of time that a sunscreen agent actually stays on the surface of the skin. *Vollhardt* does teach that his invention can also be practiced with antioxidants, anti-inflammatory compounds, anti-microbial compounds, antiperspirants, fragrances and skin whitening compounds. (*See* cols.4-5.) Accordingly, hydrocortisone is merely one of many, many other of *Vollhardt's* less preferred active agents, leaving one skilled in the art to pick and choose from a myriad of combinations in order to arrive at the presently claimed invention.

In responding to the Appellants' arguments, the Examiner has indicated that he has considered both the specification and the Fares Declaration. (Paper No. 20080325, at 4.) However, the Examiner merely repeats his prior determination that the Fares Declaration was not convincing because the "declaration sets forth only the reasoning why applicants chose pentylene glycol." (*Id.*) As discussed above, and contrary to the Examiner's view, Dr. Fares does in fact explain why he believes the claimed invention is patentable. Apparently ignoring the unexpected results shown in both the Specification and the Fares declaration, the Examiner merely repeats his assertion that he "has set forth a clear *prima facie* obviousness case with a different motivation and reasoning why pentylene glycol would be utilized." (*Id.*)

Evidence of unexpected results is rebuttal evidence provided to rebut a *prima facie* case for obviousness. Thus, the Examiner's statement that he "has set forth a clear prima facie obviousness case with a different motivation and reasoning why pentylene glycol would be utilized" (paper No. 20080325, at 4) is simply nonresponsive to the Appellants' arguments regarding the evidence of unexpected results. As previously discussed, "[o]ffice personnel should not . . . summarily dismiss [rebuttal evidence] as not compelling or insufficient. If [rebuttal] evidence is deemed insufficient to rebut the *prima facie* case of obviousness, Office personnel should specifically set forth the facts and reasoning that justify this conclusion." M.P.E.P. § 2145, at 2100-164.

By ignoring the evidence of unexpected results, the Examiner has, in effect, summarily dismissed this evidence. Accordingly, the Examiner has not met his burden to provide facts and reasoning demonstrating why the unexpected results presented in the Specification and the Fares Declaration are not sufficient to overcome the alleged *prima facie* case of obviousness.

Appellants have presented clear evidence of unexpected results both in the Specification and in the Fares Declaration. Having demonstrated unexpected results, and in view of the fact that they stand completely unrebutted by the Examiner, Appellants respectfully submit that they have demonstrated that the claimed invention is not obvious and is a patentable contribution over the prior art.

E. The Lynchpin Of The Examiner's Case, Namely *Castro*, Does Not Suggest The Present Invention

The primary ingredients in *Castro* are a self-tanning agent, a nitrogen-free polymer, and a nitrogen-free surfactant. None of these ingredients are required by the claims of the present invention. *Castro* goes on, however, to discuss the self-tanning

compositions of that patent as further comprising a cosmetically acceptable carrier. The individual components of this carrier are said to be numerous and varied, and are clearly "optional" depending upon the particular use to which these compositions are to be put. Among the 21 different categories of such ingredients, are listed dermatologically active agents and humectants, along with vehicles, which presumably include solvents for use in connection with the principal self-tanning components thereof. The pages of individual ingredients in each classification include dermatologically active agents for treating various conditions. (Col. 4 ll.61-64). Examples of these active agents include hydrocortisone, among dozens of others. There is no other discussion of the relationship between these optional components and the self-tanning agents of *Castro*, nor are any of these active agents such as hydrocortisone set forth in any specific compositions therein.

The class of "humectants" is said to be agents which promote the retention of moisture; *e.g.*, moisturizers. Among the many examples listed, including humectants from the *ICT Handbook*, is 1,2-pentanediol.

In order to obviate the present claims based on the *Castro* disclosure, one must add to the three required components of *Castro* at least two of the 21 other classes of components, for whatever reason. Then, having selected those two particular classes of components, which do not necessarily relate to each other in the *Castro* disclosure, one must then select the specific components to which the present claims are directed; namely, hydrocortisone or a derivative thereof and a solvent comprising pentylene glycol in the required amounts. Again, the dermatologically active agents of *Castro* are intended to treat specific conditions. The humectants of *Castro* are intended to promote the retention of moisture. There is no particular reason why even these broad classes of compounds would be

combined in the compositions of *Castro*, much less the particular components of the present invention in the required amounts.

In any event, the vehicles referred to in column 6, lines 44 *et seq.* of *Castro* are fluids, primarily water, which are capable of delivering the other components of these compositions to the skin. Once again, there is no reference in *Castro* to solvents such as, in particular, the pentylene glycol required by all of the claims herein.

The Examiner has never provided any particular reason why one would select from the many hundreds of potential components disclosed in *Castro* the particular ones to which the present invention is directed. The Examiner merely refers to specific portions of the specification in order to obviate the present claims, with the only basis for that selection clearly being one of pure hindsight reconstruction. In the case of *In re Baird*, 16 F.3d 380, 29 U.S.P.Q.2d 1550 (Fed. Cir. 1994), the court reversed the Examiner's obviousness rejection. In that case, the claims were directed to three specific Bisphenol A polyesters, and the cited art (*Knapp et al.*) disclosed a class of compositions, including each of the three claimed Bisphenol A compounds. In reversing the board, after recognizing that *Knapp et al.* disclosed each of the three claimed compounds, the Federal Circuit concluded that the reference "contains a large number of variables," and while it "unquestionably encompasses Bisphenol A when specific variables are chosen, there is nothing in the disclosure of *Knapp* suggesting that one should select such variables." The court also relied on the fact that the reference actually taught away from the claimed compound by focusing on other Bisphenols. It was therefore concluded that "[g]iven the vast number of diphenols encompassed by the generic diphenol formula in *Knapp* . . . we conclude that *Knapp* does not teach or fairly suggest the selection of Bisphenol A." (Citing *In re Belle*, 991 F.2d 781, 26 U.S.P.Q.2d, 1529

(Fed. Cir. 1993).) Precisely the same circumstances are presented by the citation of *Castro* in this case, where there are not only huge numbers of possible combinations and variations, but there is no particular reason to select any one or more of the optional classes of ingredients set forth therein, and certainly not the specific combination which is the subject of Appellants' claims.

Finally, there is no reference whatsoever to the amount of any of the dermatologically active agents, including hydrocortisone, sent forth in the *Castro* disclosure, and certainly not the amounts required by the claims herein. It is clear that *Castro* is not a basis for obviating the present invention. As will be seen from the discussion which follows, the combination of *Castro* with various secondary references does not alter this conclusion.

F. The Suggested Combination Of References Would Destroy The Operability Of Those Very References

The cited references disclose disparate compositions and methods and are directed to purposes that are completely incompatible with one another. The Examiner merely combines these references, without any discussion of what it is that suggests doing so in the first instance. The truth is, however, that these combinations themselves would render one or more of the prior art inventions unsatisfactory for its intended purpose. Such a combination does not, and indeed cannot, meet the Examiner's burden to establish a *prima facie* case for obviousness.

"If [a] proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." *M.P.E.P.* § 2143.01, at 2100-137 (citing *In re Gordon*, 733 F.2d 900, 221 U.S.P.Q. 1125 (Fed. Cir. 1984)). Likewise, "[i]f references taken in combination would produce a

'seemingly inoperative device,' we have held that such references teach away from the combination and thus cannot serve as predicates for a prima facie case of obviousness." *McGinley v. Franklin Sports*, 262 F.3d 1339, 1354 (Fed. Cir. 2001) (citing *In re Sponnoble*, 405 F.2d 578, 587, 160 U.S.P.Q. 237, 244 (C.C.P.A. 1969)). The combination of the cited references proposed by the Examiner violates these principles.

Castro is directed to self-tanning compositions that are effective only on the surface of the skin, hair or nails. *Cooper*, on the other hand, is directed to compositions and methods for the transdermal delivery of corticosteriods, requiring specific diols (not including the presently claimed pentylene glycol) and a cell-envelope disordering compound. *Quigley* is directed to topical antifungal compositions that minimize the amount of time on the surface of the skin and minimize the penetration of the steroid into the skin. Finally, *Vollhardt* is directed to methods of improving the water resistance (*i.e.* the amount of time on the skin) of cosmetic or dermatological compositions.

Cooper cannot be combined with either *Castro* or *Quigley* without rendering at least one of these inventions unfit for its intended purpose. *Castro* and *Quigley* are directed to agents that are active only on the skin surface. *Quigley* explicitly teaches that skin penetration by the steroid is undesirable and leads to potentially dangerous side effects. In contrast, *Cooper* is specifically directed to compositions that have enhanced skin penetration. Accordingly, to combine these references, either the compositions of *Cooper* must be made non-penetrating; rendering them useless for their intended purpose of providing transdermal or percutaneous delivery of steroids, or conversely, the compositions of *Castro* and *Quigley*

must be made skin penetrating; rendering them unsatisfactory for their intended purpose of skin surface treatment.

Similarly, *Quigley* and *Vollhardt* cannot be combined without rendering at least one of these inventions unfit for its intended purpose. *Quigley* explicitly teaches that skin penetration by the steroid is undesirable, and therefore the amount of time that the composition is present on the skin should be minimized. *Vollhardt*, on the other hand, is directed to methods of increasing the amount of time that its compositions remain on the skin, *i.e.*, increasing water resistance of sunscreens. Accordingly, in order to combine these references either the compositions of *Quigley* must be made more long lasting; rendering them useless for their intended purpose of providing minimal penetration of the steroid, or conversely, the compositions of *Vollhardt* must be modified to minimize the amount time these compositions remain on the skin; rendering them useless for their intended purpose of increasing water resistance.

In view of the foregoing, the combination of the cited references as suggested by the Examiner would render the prior art inventions unsatisfactory for their intended purposes. Accordingly, there is simply no motivation to make these combinations. *See Gordon*, 733 F.2d at 902. (reversing the decision of obviousness on the ground that the proposed modification of the prior art would have rendered the claimed invention inoperable for its intended purpose) Thus, the rejection does not present a *prima facie* case for obviousness.

G. When Appreciated For All That They Disclose The Cited References Provide No Motivation Or Suggestion That They Be Combined In The Manner Suggested By the Examiner

In making the present rejection, the Examiner has relied on only those portions of the cited references that support his

position and has apparently ignored the remainder of these disclosures. When the disclosures of the cited references are read objectively, and in their entireties, however, there is nothing to motivate one of skill in the art to combine the references in the manner suggested by the Examiner, so as to arrive at the claimed compositions.

Prior art publications must be evaluated in their entirety. It is impermissible within the framework of 35 U.S.C. § 103 to pick and choose from the references only so much as will support a given position to the exclusion of other parts of the references necessary to the full appreciation of what such references fairly suggest to one skilled in the art. *See In re Mercer* 515 F.2d 1161, 1165-66, 185 U.S.P.Q. 774, 778 (C.C.P.A. 1975). This impermissible picking and choosing is exactly what the Examiner has done in this rejection.

The Examiner has alleged that *Castro* discloses "topical compositions comprising 1,2-pentanediol, and additional glycol (2-methyl-1,3-propane diol), and a dematologically active agent (which could be hydrocortisone or triamcinolone)." (Paper 20080325, at 7-8.) *Castro* actually discloses self-tanning compositions "comprising a self-tanning agent, a nitrogen-free polymer, and a nitrogen-free surfactant." (Col.1 ll.40-42.) *Castro* goes on to disclose that its compositions may be in the form of a cosmetic product including a cosmetically acceptable carrier, which can optionally include one or more of the separate classes of components discussed above. (Col.3 ll.39-51.) Among these disclosed classes are dermatologically active agents and humectants. Over 60 dermatologically active agents are disclosed, including hydrocortisone. (Col.4 l.64 to col.5 l.16.) Fourteen humectants, as well as others from the *ICT Handbook* are disclosed, including 1,2-pentanediol. (Col.5 ll.49-54.)

Castro does not disclose or suggest a composition containing 1,2-pentanediol and hydrocortisone. To arrive at the claimed invention, one of skill in the art must choose from the laundry list of 21 separate classes of purely optional carrier components those two that support the rejection (*i.e.*, dermatologically active agents and humectants). There is no reason why one would actually select components from these two classes, or why one would thus select a dermatologically active agent and a humectant in the first instance. However, even having selected these two classes, the skilled artisan must then choose hydrocortisone from a list of over 60 dermatologically active agents, and 1,2-pentenediol from the lengthy list of humectants. *Castro* offers no motivation or suggestion to select these particular active agent and humectant combinations, and the rejection points to none. Instead, one of skill in the art is left to pick and choose from a multitude of combinations in order to arrive at the presently claimed invention.

The Examiner has alleged that *Vollhardt* discloses "cosmetic and/or dermatological formulations comprising 1,2-pentanediol and at least one cosmetic or dermatological active agent . . . that the cosmetic or dermatologically active agent can be a steroidal anti-inflammatory such as hydrocortisone . . . [and] that 1,2-pentanediol confers greater water resistance to the compositions as compared to 1,2-propanediol and 1,2-hexanediol." (Paper No. 20080325, at 7.) *Vollhardt*'s primary objective was to increase the amount of time that a sunscreen agent stays on the surface of the skin. In the alternative, *Vollhardt* discloses that its invention may also be practiced with cosmetic an/or dermatological formulations comprising cosmetic and/or dermatological active agents(s)." (Col. 4, l. 52-56.) The classes of actives disclosed by *Vollhardt* include antioxidants, anti-inflammatory compounds, anti-microbial compounds,

antiperspirants, fragrances and skin whitening compounds. (*See* col.4 l.57 to col.5 l.58.) Among the anti-inflammatory compounds disclosed is hydrocortisone. (*See* col.4 l.67.) Thus, hydrocortisone is but one of a long list of other, less preferred active agents. As with *Castro*, one of skill in the art is left to pick and choose from a myriad of combinations in order to arrive at the presently claimed invention. (*See Baird, supra*.)

The Examiner has alleged that *Cooper* "discloses topical pharmaceutical corticosteroid compositions including 1,2-propanediol, 1,3-propanediol, 1,2-butanediol, 1,3-butanediol, 1,4-butanediol or mixtures of these diols . . . [and] that the topical pharmaceutical corticosteroids used in the compositions include hydrocortisone, hydrocortisone butyrate, hydrocortisone acetate, triamcinolone, and triamcinolone acetonide." (Paper No. 20080325, at 8.) The Examiner failed to acknowledge, however, that *Cooper* discloses that "[s]urprisingly, it has been discovered that a select number of combinations of a binary penetrator system comprising a cell-envelope disordering compound and a diol compound . . . can consistently and dramatically improve the topical delivery of certain corticosteroids . . . ." (Col. 2 l.68 to col.3 l.9.)

The only diols disclosed in *Cooper* are C_3-C_4 diols, *i.e.*, "1,2-propanediol, 1,3-propanediol, 1,2-butanediol, 1,3-butanediol, 1,4-butanediol or mixtures of these diols compounds." (Col.8 ll.56-60.) One of skill in the art having considered the entire disclosure of *Cooper* would have no motivation whatsoever to ignore the teaching thereof to employ C_3-C_4 diols, and instead, use the claimed C_5 pentylene glycol.

In light of *Cooper's* clear preference for C_3-C_4 diols, there also can be no motivation to combine *Cooper* with *Vollhardt*. As discussed above, *Vollhardt* discloses only 1,2-pentanediol, and

discloses that it is superior to the 1,2-propanediol favored by *Cooper*. Thus, one of skill in the art would find no motivation to combine *Cooper* and *Vollhardt*.

The Examiner has alleged that *Quigley* discloses "topical formulations . . . comprising a steroid . . . and propylene glycol . . ., wherein the steroid can be triamcinolone acetate." (Paper No. 20080325, at 6-7.) The Examiner, however, once again fails to acknowledge that the glycol solvents disclosed by *Quigley* are "propylene glycol, butylene glycol, hexylene glycol, polyethylene glycols, [and] polypropylene glycols." (Col.2 ll.55-57.) Thus, *Quigley* is conspicuously silent as to pentylene glycol-propylene glycol (C_3), butylene glycol (C_4), hexylene glycol (C_6) are disclosed, but pentylene glycol (C_5) is not. Thus, one of skill in the art with knowledge of the entire disclosure of *Quigley* would not only have no motivation whatsoever to use pentylene glycol, but would necessarily need to ignore the numerous glycols which are disclosed in *Quigley*, and instead choose an entirely undisclosed glycol in order to arrive at the claimed invention.

In light of the nature of *Quigley's* disclosure, there also can be no motivation to combine *Quigley* with *Vollhardt*. As discussed above, *Vollhardt* discloses only 1,2-pentanediol, which is said to be superior to the propylene glycol and hexylene glycol favored by *Quigley*. Thus, one of skill in the art would find no motivation in *Quigley* and *Vollhardt* for their combination.

Moreover, *Quigley* discloses that penetration of the steroid through the skin can lead to undesirable and potentially dangerous side effects. (Col.1 ll.27-32.) Thus, *Quigley* discloses that among the advantages of its formulation is that its compositions are quick acting and require much less residence time on the skin, and that it "minimizes the penetration of the skin with respect to the steroid." (*See*

col.2 ll.16-27.) Thus, to combine *Quigley* with *Cooper*, which teaches only skin penetrating steroid compositions, one of skill in the art must ignore the explicit teachings of *Quigley* that penetration of the steroid is to be avoided. Similarly, to combine Quigley with *Vollhardt*, which teaches a method of increasing the amount of time the composition remains on the skin, one of skill in the art must ignore the explicit teachings of *Quigley* that the composition should be kept on the skin for as short a time as possible. Accordingly, there is no motivation to combine *Quigley* with either *Cooper* or *Vollhardt*.

Thus, for the above reasons, when considered in their entireties, the disclosures of the cited references provide no suggestion or motivation to combine them in the manner suggested by the Examiner. Absent such motivation or suggestion, the cited references simply do not support a *prima facie* case for obviousness.

VIII. CONCLUSION

In light of the above discussion, Appellants request that the pending rejections be reversed, and the claims allowed to issue as presented.

Dated: November 18, 2008 Respectfully submitted,

By _____
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CLAIMS APPENDIX

16. A cosmetic or dermatological composition comprising hydrocortisone, or a derivative thereof, and a solvent for said hydrocortisone comprising pentylene glycol, wherein said hydrocortisone is present in an amount of about 0.01% to about 5% by weight of said composition.

17. The composition of claim 16, comprising a hydrocortisone derivative which is hydrocortisone acetate.

18. The composition of claim 16, comprising a hydrocortisone derivative which is hydrocortisone butyrate.

19. The composition of claim 16, wherein the amount of hydrocortisone is about 0.1% to about 5.0% by weight of said composition.

20. The composition of claim 16, wherein the amount of hydrocortisone is 4% or less by weight of said composition.

21. The composition of claim 16, wherein the amount of hydrocortisone is about 1% by weight of said composition.

22. The composition of claim 16, further comprising at least one additional solvent other than pentylene glycol.

23. The composition of claim 22, wherein said at least one solvent is a glycol.

24. The composition of claim 22, wherein said at least one solvent is butylene glycol.

25. The composition of claim 22, wherein said at least one solvent is propylene glycol.

26. The composition of claim 22, wherein said at least one solvent comprises butylene glycol and propylene glycol.

27. The composition of claim 16, wherein amount of pentylene glycol is about 5 to about 70% by weight of said composition.

28. The composition of claim 16, wherein amount of pentylene glycol is about 5 to about 25% by weight of said composition.

29. The composition of claim 22, wherein amount of said at least one additional solvent other than pentylene glycol is about 10% to about 70% by weight of said composition.

30. The composition of claim 16, which is an emulsion.

31. The composition of claim 16, which is a gel.

32. The composition of claim 16, which is an ointment.

33. The composition of claim 16, which is a lotion.

34. The composition of claim 16, which is a shampoo.

35. A method of formulating hydrocortisone or a derivative thereof for use in a cosmetic or dermatological composition, comprising mixing said hydrocortisone in an amount of about 0.01% to about 5% by weight of the composition, and a solvent for said hydrocortisone comprising pentylene glycol.

36. A method of formulating a hydrocortisone or derivative thereof for use in a cosmetic or dermatological composition, comprising mixing said hydrocortisone or a derivative thereof in an amount of about 0.01% to about 5% by weight of the composition, and a solvent for said hydrocortisone comprising pentylene glycol.

37. A method of treating skin or scalp, comprising applying to skin or scalp a composition comprising hydrocortisone or a derivative thereof, and a solvent comprising pentylene glycol, wherein said hydrocortisone is present in an amount of about 0.01% to about 5% by weight of said composition.

38. A method of treating skin or scalp, comprising applying to skin or scalp a composition comprising hydrocortisone or a derivative thereof, and a solvent for said hydrocortisone comprising pentylene glycol, wherein said hydrocortisone is present in an amount of about 0.01% to about 5% by weight of said composition.

EVIDENCE APPENDIX

1. Declaration Under 37 C.F.R. § 1.132 of Hani Fares, Ph.D. submitted to the United States Patent and Trademark Office with an Amendment dated March 29, 2005.

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date shown below.

Dated: 3/29/15 Signature: Shawn P. Foley
(Shawn P. Foley)

Docket No.: LOREAL 3.0-039
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of: Fares et al.	
Application No.: 10/646,300	Group Art Unit: 1617
Filed: August 22, 2003	Examiner: Williams, Leonard M.
For: COMPOSITIONS CONTAINING TOPICAL ACTIVE AGENTS AND PENTYLENE GLYCOL	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. §1.132

I, Hani Fares, do declare as follows:

I received a Doctor of Philosophy degree in Pharmaceutics from Rutgers University in 1997.

I have more than 15 years of experience in the fields of cosmetics and dermatology, particularly from the standpoint of cosmetic and dermatological formulations.

I have been employed by Loreal, S.A. for more than 3 years, and have held the title of Manager since 2005.

I am a named co-inventor of the captioned patent application.

I have reviewed the Office Communication mailed January 11, 2005, and the four publications cited therein, namely U.S. Patents 6,113,888 to Castro, *et al.* ("*Castro*"); U.S. Patent 4,552,872 to Cooper, *et al.* ("*Cooper*"); U.S. Patent 6,075,056 to Quigley, *et al.* ("*Quigley*"); and U.S. Patent 6,274,124 to Vollhardt ("*Vollhardt*").

I disagree with the determination reached by the Examiner that claims of the patent application would have been obvious over *Castro*, in view of *Cooper* and *Quigley*, and further in view of *Vollhardt*. In my opinion, no one claim of this patent application would have been obvious in view of the collective teachings of these four patents.

In my opinion, the teachings of *Cooper* would not have motivated a person skilled in the art to include pentylene glycol in a topical cosmetic or dermatological composition with a reasonable expectation that it would have enhanced penetration and uptake of a cosmetic or dermatological active agent. Although not explicit, *Cooper's* limitation to C3-C4 diols would have discouraged use of a C5 diol. My co-inventors and I, however, proceeded contrary to *Cooper's* teachings.

The invention disclosed in *Vollhardt* is directed to a method for imparting water resistance or to improving water resistance of a cosmetic or dermatalogical formulation containing a sunscreen agent or other active agent, by adding a water resistance enhancing effective amount of 1,2-pentanediol to an otherwise cosmetic or dermatological formulation that contains at least one cosmetic and/or dermatological active agent in a cosmetically and/or pharmaceutically acceptable carrier, for topical application to the skin of humans. On Column 3, lines 10-14, *Vollhardt* teaches that with respect to formulations comprising cosmetic and/or dermatological active agent(s) other than UV protectants, the term "water resistance" refers to the activity or effect over time of the respective agent of a formulation subjected (after application to the skin) to contact with water. When read in the context of the entire patent disclosure, including the background section, I take this statement to mean that when applied to human skin in a formulation containing 1,2-pentanediol, the active agent is not as easily washed off, and has a higher retention on human skin

upon contact with water or other aqueous solutions, than it would have in the absence of pentylene glycol.

We sought to increase solubility of hydrocortisone and the rate and/or extent of penetration through the skin barrier, and in so doing, unexpectedly discovered that hydrocortisone is more soluble in pentylene glycol than in other diols. The claimed invention achieves unexpected results, namely greater aesthetic appeal, less tackiness, and greater penetration and bioavailability of hydrocortisone, compared to other commercial hydrocortisone topical formulations. Increasing water resistance and retention on the skin, which were *Vollhardt*'s objectives, are completely different and even opposite the properties we were seeking, namely increased solubility, penetrability and bioavailability.

I declare under penalty of purjery that the foregoing is true and correct.

Date: March 28, 2005

HANI FARES

RELATED PROCEEDINGS APPENDIX

None known at this time.

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